SOUTH AFRICAN HEALTH PRODUCT REGULATORY AUTHORITY

SAHPRA
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HEALTH PRODUCTS
REGULATORY AUTHORITY

PRE-REGISTRATION CONSULTATION MEETING

This document provides guidance on the procedures involved in the scheduling and conduct of Pre-Registration Consultation meetings between the Office of the Chief Regulatory Authority (CRO) of the South African Health Product Regulatory Authority (SAHPRA), and the applicant / sponsor for biological medicines. The primary purpose of the meetings is to address issues relating to the development of biological medicines in the planning phase of such products.

Guidelines and application forms are available from the office of the CRO and on the SAHPRA website.

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SAHPRA CEO

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1 PURPOSE

The purpose of this guidance document it to describe the procedures involved in the scheduling and conduct of Pre-Registration Consultation (PRC) meetings between the Office of the CRO of the SAHPRA and the applicant / sponsor of biological medicines. The primary purpose of the meetings is to address issues relating the development of a product in the planning phase of such products.

2 SCOPE

This guideline applies to the scheduling of a PRC meeting by the parties involved in the development or manufacturing of biological medicines that have not been previously submitted for registration to the MCC, or to any other regulatory authority and for which registration may be sought from the MCC in the future.

PRC meetings with industry provide a forum for SAHPRA to provide guidance to organizations during product development and facility design, and to facilitate their compliance with the regulations governing the development of products.

This should be limited to local manufacturers and developers of biological medicines, including vaccine developers where the major part of the clinical development will be in a South African population.

Meetings should serve a useful purpose, and should not be premature or clearly unnecessary. In order to guide the meeting, a check-list is to be submitted with the request for a meeting.

3 TERMS, DEFINITIONS AND ABBREVIATIONS

3.1 Applicant/Developer/Sponsor

The legal entity (or agent) that applies for the permit to conduct clinical trials, and eventually for the registration of the new biological medicine.

3.2 Pre-Registration Consultation (PRC) Meeting

Meeting requested by developer at the point where the manufacturing process for a potential product has reached a point of consistency and has a potentially defined presentation/indication, but further development could benefit from the advice of regulatory experts on the pre-clinical or clinical development plan; the consultation might enable applicant/s to submit dossiers containing appropriate information in line with the CTD format, and which may lead to an appropriately constructed dossier that will enable a decision on registration of a biological medicine.

3.3 Pre-Registration Consultation Expert Committee (PRC EC)

Core team of regulatory reviewers focused on the quality and clinical development of a particular product, providing the core input to both the Clinical Trials Committee (CTC) and Biological Medicines Committee (BMC) when the application comes up for review. The EC operates separately from the CTC. It predominantly focuses on product development, leaving issues of trial conduct and relevant ethics review bodies to the CTC.

3.4 Pre-Registration Consultation (PRC) Meeting Material

Dossier to be compiled and submitted before a consultation meeting is conducted

3.5 Pre-Registration Consultation (PRC) number

Unique number identifying the product/presentation, including the dossier submitted for a Pre-Registration Consultation meeting. Each communication from MCC to applicant gets the PRC plus a suffix number identifying the sequence of communication, e.g. 334455/001, 334455/002.

3 Terms, definitions and abbreviations - continued

3.6 Point of Contact (POC)

Person at SAHPRA identified as responsible to assist the applicant with the procedure to schedule and coordinate a meeting.

4 TYPES OF PRC MEETINGS

Summary: *Three types of meetings have relevance. Type A: meeting conducted before finalization of non-clinical tests. This is not a formal submission. Type B: meeting conducted when non-clinical development is complete and Ph-I trials are ready for submission. This is a formal submission. Type C: These meetings are held during the clinical development phase and prior to final registration application.*

4.1 TYPE A

a. To review and reach agreement on the format of application.
b. Design of animal studies needed to support human clinical testing and product characterization issues.
c. The scope and design of planned Phase I studies.
d. Facility design.
e. General product issues.

4.2 TYPE B

a. Depict for reviewers the general information to be submitted in the registration application.
b. Discuss preliminary efficacy results derived from studies conducted to support registration process and appropriate methods for final statistical analysis.
c. Discuss the proposed format for data in the planned marketing application.
d. To identify the studies that the sponsor/applicant will rely on as adequate and well-controlled.
e. Plans to assess paediatric safety and effectiveness.
f. To discuss submission of an incomplete application.
g. To discuss any major outstanding issues.

4.3 TYPE C

To discuss the Phase II or Phase III clinical development of a proposed Medicinal Product. This would typically be conducted by the PRC EC, with attendance by CTC members.

4.3.1 End of Phase I / Pre Phase II meeting

a. To review Phase I clinical testing data.
b. To reach agreement on design of Phase II controlled clinical trials with the goal that such testing will be adequate to provide sufficient data on the medicine's safety and effectiveness to support a decision on its approvability for marketing, and to discuss the need for, as well as the design and timing of, studies of the biological medicine in paediatric patients.

4.3.2 End of Phase II / Pre-Phase III meeting:

a. Review Phase II data to determine if it is safe to proceed to Phase III.
b. To evaluate plans for the Phase III program and protocols.
c. Plans to assess paediatric safety and effectiveness
d. To identify any additional information necessary to support a registration application for the uses under investigation.

5 PROCEDURE FOR REQUEST TO SCHEDULE MEETINGS

5.1 All communications regarding meetings, as defined in this document, should be forwarded to the Registrar's office.

5.2 All meetings must be preceded by the submission of a written application to the Registrar of Medicines and be accompanied by the necessary discussion materials.

5.3 Approximate lead-time for submission of information package in CTD format is approximately one (1) month before the scheduled meeting with the Expert Committee.

5.4 Every effort to respond to meeting requests will be made by SAHPRA as expeditiously as possible.

5.5 Upon receipt of a request for consultation with the relevant Expert Committee of the SAHPRA, the CRO will appoint an appropriate qualified Panel (max 6 persons) to conduct the consultation.

5.6 Meetings may either be face-to face (in person) or electronic i.e. teleconference or video conference/Skype.

5.7 Meetings will be strictly limited to one (1) hour and will result in a verbal response from the Panel at the conclusion of the meeting.

5.8 These responses are non-committal and are non-binding on the CRO or on SAHPRA.

6 PRE-REGISTRATION CONSULTATION MEETING MATERIAL

A completed PRC meeting Material Checklist must be submitted with the application.

7 CANCELLATION OF MEETING

7.1 The POC must clearly convey to the Applicant that all the pre-read meeting material (Dossier) should be received not less than one (1) month prior to the scheduled meeting.

7.2 The applicant should also be notified that failure to submit adequate meeting materials by the appropriate date could result in cancellation.

7.3 Meetings may be postponed or cancelled by either party based on sufficient cause. All parties need to be immediately notified and a cancellation notice shall be forwarded by Fax or e-mail via the Registrar's office.

8 THE MEETING

8.1 The POC shall ensure that a clear agenda and adequate materials are available for the PRC meeting.

8.2 The agenda for the sponsor /applicant's question and SAHPRA responses as generated in the internal pre-meeting.

8.3 The meeting will begin with introductions.

8.4 The appointed meeting leader or rapporteur will keep the meeting to the agenda with attention to the time allotted and summarize issues and /or agreement reached at the conclusion of the meeting.

8.5 In order to decrease misunderstandings, it is strongly recommended that the last 5 – 10 minutes of the meeting be used to summarize agreements reached, advice provided, action items, and unresolved issues.

8 Meeting - continued

8.6 Minutes of the meeting.

a. The secretariat will not provide minutes of the meeting to the applicant, but will retain notes for own use as compiled by the POC.

b. The applicant takes minutes for own reference and also submit such to the POC for approval as a true reflection of proceedings.

c. In exceptional cases, the Panel / Expert committee may need to respond to the applicant in writing or in a follow-up meeting. Written material will take the form of an Expert Opinion or Advisory Statement.

d. In the event of the Developer intending to submit a Clinical Trial Application to the CTC following consultation with the PRC EC; the PRC EC report will be provided to CTC.

9 REFERENCES

Selected bibliography and supporting documentation to the PRC proposal

9.1 Guidance for Industry. Formal Meetings Between the FDA and Sponsors or Applicants
http://www.fda.gov/downloads/Drugs/Guidances/ucm153222.pdf

9.2 Formal FDA Meeting Request: Guidance and Template (contains further links to relevant FDA guidance documents)
http://ictr.johnshopkins.edu/wp-content/uploads/import//1331-FDA%20Formal%20Meeting%20Guidance%20and%20Template.pdf

9.3 Pre-IND Meeting Checklist (contains further links to relevant FDA guidance documents)
http://icahn.mssm.edu/static_files/MSSM/Files/Research/Resources/Office%20of%20Clinical%20Research/PreIND-Meeting-Checklist.pdf

9.4 European Medicines Agency Guidance for Companies requesting Scientific Advice and Protocol Assistance
http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004089.pdf
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000049.jsp&mid=WC0b01ac05800229b9

9.5 CHMP <Protocol Assistance> <Scientific Advice> Briefing Document Template (18/06/2010)
Template letter of intent for request of scientific advice or protocol assistance (08/11/2012)
http://www.ema.europa.eu/docs/en_GB/document_library/Template_or_form/2009/11/WC500011910.pdf

10 UPDATE HISTORY

Date	Reason for update	Version & publication
June 2014	First version approved for implementation	Version 1, March 2015
March 2015	Date of implementation	